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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/515,983	09/30/2005	Elan David Massey	RD 440	6315

22884 7590 09/02/2009

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EXAMINER	
MA, JAMESON Q	
ART UNIT	PAPER NUMBER
1797	
MAIL DATE	DELIVERY MODE
09/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/515,983	MASSEY ET AL.	
	Examiner	Art Unit	
	JAMESON Q. MA	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-27,29-38 and 40-43* is/are pending in the application.

4a) Of the above claim(s) *37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-27, 29-36, 38, and 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 November 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed on 5/5/2009 is acknowledged.

2. Claim 37 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 5/5/2009.

Specification

3. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: the frictional lock of claim 24 is not described in the specification.

Drawings

4. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the locking mechanism of claims 22-24 and the pumps of claims 25-27 must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure

is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 17 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 17 recites the limitation "the top surface" in line 2. There is insufficient antecedent basis for this limitation in the claim. Further, it is unclear as to which component or structure in the claimed apparatus the top surface refers to.

8. Claim 36 is indefinite because of its use of a trademark. A trademark or tradename is an identification of a supplier and not a definite object. The trademarks should be replaced with generic terminology that clearly identifies the particular material(s).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 2, 7-8, 11-12, 14-18, 21-22, 24, 29, 35, 38, and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Stoppini et al. (US 5,958,762).

Regarding claims 2, 38, and 43, Stoppini discloses an exposure device comprising a base portion (1) connected with a top portion (3) to form therebetween a medium chamber adjacent said base portion, a fluid exposure chamber adjacent said top portion, and a plurality of cell culture chambers (6) positioned between said medium chamber and said culture chamber (see fig. 1: the medium chamber is viewed to be the space below membrane 5, and the fluid exposure chamber is the space above membrane 5), said medium chamber being common to all culture chambers. The device further comprises a fluid inlet and outlet (sealing devices 4 and 4' are viewed as fully capable of acting as an inlet or outlet, as fluid flow could be initiated via a syringe or similar device) and a medium inlet and outlet (sterile septa 9' and 9" are viewed as medium inlets/outlets).

The top surface of the bottom portion of the device (as viewed in figure 1), is viewed as a medium directing means.

For claim 7, the device comprises three culture chambers.

For claim 8, the base of said culture chambers are spaced apart from the base of said device by a gap, which would allow nutrient medium to flow freely under the chambers.

For claim 11, the medium inlet is located in said base portion of said device.

For claim 12, the medium inlet is located in a sidewall of said base portion.

For claims 14-18, the medium inlet is viewed as a tube, the medium outlet is spaced apart from the inlet by all of said culture chambers and the medium outlet is viewed as fully capable of removing nutrient medium from a top surface.

For claims 21-22, the medium outlet is viewed as a tube and as locked into said device by a locking mechanism.

For claim 24, the locking mechanism is viewed as a frictional lock.

For claim 29, the fluid exposure chamber is in flow communication with all said culture chambers.

For claim 35, the device further comprises a cell culture chamber support (membrane surface 8 is viewed as a support).

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 9-10, 13, and 19-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762).

Regarding claims 9-10, Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the length of the gap between the culture chambers and base portion. As the amount of nutrient medium and thus total nutrients available to the culture chambers are variables that can be modified, among others, by adjusting said gap length, amount of nutrient medium and thus total nutrients available to the culture chambers as the gap length is increased, the precise gap length

would have been considered a result effective variable by one having ordinary skill in the art at the time the invention was made. As such, without showing unexpected results, the claimed gap length cannot be considered critical. Accordingly, one of ordinary skill in the art at the time the invention was made would have optimized, by routine experimentation, the thickness of the gap length in the apparatus of Stoppini to obtain the nutrient medium (and thus total nutrient capacity) of the device (In re Boesch, 617 F.2d. 272, 205 USPQ 215 (CCPA 1980)), since it has been held that where the general conditions of the claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. (In re Aller, 105 USPQ 223).

Regarding claim 13, Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the medium inlet located in a bottom wall of the base portion. The reference only discloses the inlet in a side wall of the base portion. However, the placement of the medium inlet is strictly an engineering design choice that would have been obvious to one of ordinary skill in the art barring any unexpected results based on the exact placement of the inlet. **Specifically, a change in the placement of the inlets would create two identically functioning and thus equivalent embodiments.** Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to place the medium inlet in the bottom wall of the base portion of the device.

Regarding claims 19-20, Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose the medium outlet comprises two outlets. However, it would have been obvious to one of ordinary skill in the art at the

time of invention to add an additional medium outlet in a separate location of the device in order to allow for quicker and more efficient medium removal. Additionally, regardless of the placement of the second (or more) outlet(s), they would necessarily be positioned to allow for both basal and submersion feeding of cell cultures within the cell culture chambers.

Claims 3-6 and 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762) in view of Minchinton (US 5,602,028).

Regarding claims 3-6 and 40-42, Stoppini discloses all of the claim limitations as set forth above. However, the reference does not explicitly disclose the device wherein the medium directing means is formed from a raised area of said base portion of said exposing device.

Minchinton discloses a similar device to Stoppini which comprises three cell culture chambers comprising a semi-permeable membrane. Minchinton also discloses that the chamber includes stirring means at the base of the chamber to vigorously stir the liquid medium and move said medium to flow over both major surfaces of the membrane at a speed to adequately deliver nutrients to the cell culture adhered to and growing on one major surface of the membrane (see C2/L38-50 and fig. 1). The stirring means is disclosed as a magnetic stir bar (34).

As a magnetic stir bar would be capable of achieving fluid flow faster than some commercially available peristaltic pumps, it would have been obvious to one of ordinary skill in the art at the time of invention to incorporate into the device of Stoppini, a

magnetic stir bar in order to generate sufficient fluid flow speeds to adequately fulfill the nutrient needs of particular cell cultures, as taught by Minchinton.

The magnetic stir bar of modified Stoppini is viewed as a raised area of said base portion of the device and as an island within the medium chamber. It is further viewed as centrally located within the medium chamber and located equidistant to each of said culture chambers.

15. Claims 23 and 30-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762) in view of Aufderheide et al. (A method for in vitro analysis of the biological activity of complex mixtures such as sidestream cigarette smoke) and Rose et al. (US 4,792,378).

Regarding claims 30-34, Stoppini discloses all of the claim limitations as set forth above. The reference does not explicitly disclose an additional fluid dispersing means. Aufderheide discloses that studies of the cytotoxicity of air contaminants such as gaseous particles have traditionally used animal experiments because of the difficulties in exposing cell cultures directly to these substances (see abstract). Aufderheide further discloses that the Cultex system allows for the direct exposure of cigarette smoke to human bronchial epithelial cells to allow does-dependent effects to be measured (see abstract).

Rose discloses a gas dispersion disk (20) that includes an arrangement of apertures which are tailored to the particular pressure gradients existing within a reactor chamber to thereby provide a uniform flow of gas vapors to the various objects below it (see C4/L52-63).

It would have been obvious to one of ordinary skill in the art at the time of invention to provide a gas (fluid) dispersing means in a portion of the device of Stoppini, in order to provide a means for in vitro toxicology testing. This would allow for the dose-dependent measurement of cigarette smoke effects to human bronchial cell in vitro, as taught by Aufderheide. It would have further been obvious to one of ordinary skill in the art at the time of invention to use the fluid dispersion disk of rose in the apparatus of modified Stoppini, in order to create a uniform distribution of gas (fluid) flow over the cell cultures. The use of a dispersion disk would necessitate that it be located above the cells to allow for uniform flow distribution.

Aufderheide further teaches that the fluid inlet is connected to a fluid generating means (see figure 7: smoking machine).

Regarding claim 23, Stoppini discloses all of the claim limitations as set forth above, but the reference does not explicitly disclose that locking mechanism of the fluid outlet is a threaded screw arrangement having a central bore.

Aufderheide discloses that a Cultex system is used to study smoke effects (figs. 5-7). The Cultex system comprises outlets with a screw arrangement having a central bore. It would have been obvious to one of ordinary skill in the art to substitute the septa medium outlet of Stoppini with a screw arrangement having a central bore as taught by Aufderheide, because doing so would allow a more rigid port to connect tubing for fluid disposal.

16. Claims 25-27 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stoppini et al. (US 5,958,762) in view of Gruenberg (US 5,627,070).

Regarding claims 25-27, Stoppini discloses all of the claim limitations as set forth above. Additionally, the reference discloses that perfusion of the nutritive medium takes place by means of an external peristaltic pump (see C2/L40-44). However, the reference does not explicitly disclose that there are two separate pumps attached to the medium inlet and outlet respectively.

Similar to Stoppini, figure 1 of Gruenberg teaches a cell growing device for in vitro cell population growth (see abstract). The device contains a recirculation mechanism (6), which contain stainless steel connectors (6a) which connect the inflow and outflow openings of cartridges (4, which are where the cells are maintained), see C10/L24-43). A centrifugal pump (44a) carries media through the stainless steel pathway to a regeneration mechanism (46) wherein media is replenished with nutrients and essential gases, and wherein waste products from cell growth are removed. A second pump (44b) directs the regenerated media to the cartridge inflow openings.

It would have been obvious to one of ordinary skill in the art at the time of invention to substitute the peristaltic pump of Stoppini, with the dual-pump recirculation/media regeneration system in order to allow the circulating media to be replenished, as taught by Gruenberg.

The two centrifugal pumps would be fully capable of operating at separate pump rates. Regarding the limitations of claim 27 which are directed to a manner of operating disclosed pump, it is noted that neither the manner of operating a disclosed device nor material or article worked upon further limit an apparatus claim. Said limitations do not differentiate apparatus claims from prior art. See MPEP § 2114 and 2115. Further, it

has been held that process limitations do not have patentable weight in an apparatus claim. See Ex parte Thibault, 164 USPQ 666, 667 (Bd. App. 1969) that states "Expressions relating the apparatus to contents thereof and to an intended operation are of no significance in determining patentability of the apparatus claim."

Regarding claim 36, Gruenberg teaches that the recirculation tubing is made from stainless steel, as disclosed above. Therefore, part of the exposure device is made from stainless steel.

Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMESON Q. MA whose telephone number is (571)270-7063. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571)272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael A Marcheschi/
Supervisory Patent Examiner, Art Unit 1797

JM
August 24, 2009